Supplementary Table 1: Definition of primary outcome events

Event	Outcome definition	Objective diagnostic test
VTE		
DVT	- Acute symptomatic lower or upper extremity DVT - Acute incidental proximal DVT - Catheter related DVT	duplex / compression ultrasonography, contrast venography or positive in autopsy
PE	- Acute symptomatic PE - Acute incidental PE of the segmental or more proximal pulmonary arterial branches	CTPA, ventilation/perfusion lung scan, magnetic resonance pulmonary angiography, invasive angiography or positive in autopsy
Fatal PE	- Death under the objectified diagnosis of acute PE - Death under the clinical suspicion for PE (PE not ruled out as a cause)	- objective diagnosis of PE and death in the immediate course of the event - positive in autopsy - patients who have died under the clinical signs and symptoms of PE
Visceral vein thrombosis	- Acute symptomatic or incidental visceral vein thrombosis if treated with anticoagulation	- CT/CTA - MR/MRA
ATE		
Acute coronary syndrome (ACS)	- STEMI (ST-elevation myocardial infarction) - NSTEMI (non-ST-elevation myocardial infarction) - unstable angina pectoris	abnormal cardiac biomarkers (cardiac troponin I/T above the 99th percentile) in the setting of evidence of acute myocardial ischemia (new ischemic ECG changes; development of pathological Q waves; imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology; identification of a coronary thrombus by angiography or autopsy
Acute peripheral artery occlusion	- acute thrombotic occlusion if treated with interventional procedure of non-cardiac arteries excluding intracranial vessels	Duplex ultrasonography, CTA, MRA, invasive angiography (DSA) Interventions include catheter-based or open surgical procedures
Ischaemic stroke	- Minor stroke (National Institute of Health Stroke	- CT/CTA - MR/MRA

	Score ≤ 3) - Major stroke (National Institute of Health Stroke Score > 3)	

ACS indicates acute coronary syndrome; ATE, arterial thrombotic event; CT, computed tomography; CTA, computed tomography angiogram; CTPA, computed tomography pulmonary angiogram; DSA, Digital subtraction angiography; DVT, deep vein thrombosis; ECG, electrocardiogram; MR, magnetic resonance imaging; MRA, magnetic resonance angiography; NSTEMI, non-ST-elevation myocardial infarction; PE, pulmonary embolism; STEMI, ST-elevation myocardial infarction; and VTE, venous thromboembolism.

Supplementary Table 2: Secondary outcome definitions

Outcome event	Outcome definition
Overall survival (OS)	Time from therapy initiation to death from any cause
Progression free survival (PFS)	Time from therapy initiation to radiological disease progression according to iRECIST[1] or death from any cause
Disease control rate (DCR)	Proportion of patients with complete remission, partial remission, or stable disease according to iRECIST[1] as best radiological response during immune checkpoint inhibitor therapy
Major bleeding (MB)	Defined according to the ISTH classification[2]: - Fatal bleeding - Symptomatic bleeding in critical site / organ* - Bleeding causing drop in haemoglobin level of ≥20 g/L or leading to transfusion of ≥2 units of whole blood or red cells
Clinically relevant non-major bleeding (CRNMB)	Defined according to the ISTH classification[3]: - Bleeding requiring medical intervention - Bleeding resulting in hospitalization - Bleeding prompting face-to-face evaluation - Not fulfilling criteria for major bleeding

*: Critical sites or organs include intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial, and intramuscular bleeding with compartment syndrome.

ISTH indicates International Society on Thrombosis and Haemostasis; and iRECIST immunotherapy-specific response evaluation criteria in solid tumours.

Supplementary Table 3: Anticoagulation and anti-platelet therapy at baseline

Variable	Count (%)
Patients on continuous anticoagulation at baseline	111 (16.5%)
Indication for anticoagulation	
- Atrial fibrillation	42 (37.8%)
- Prior cancer-associated VTE	40 (36.0%)
- Prophylactic anticoagulation	16 (14.4%)
- Prior VTE unrelated to cancer	7 (6.3%)
- Other*	6 (5.4%)
Anticoagulation agent	
- Enoxaparin	38 (34.2%)
- Rivaroxaban	25 (22.5%)
- Phenprocoumon	18 (16.2%)
- Apixaban	13 (11.7%)
- Edoxaban	13 (11.7%)
- Dabigatran	4 (3.6%)
Patients on continuous anti-platelet therapy at baseline	133 (19.8%)
Indication for anti-platelet therapy†	
- Coronary artery disease	50 (37.6%)
- Peripheral artery disease	42 (31.6%)
- Prior myocardial infarction	26 (19.5%)
- Prior Stroke / TIA	15 (11.3%)
Anti-platelet agent	
- Aspirin	118 (88.7%)
- Clopidogrel	11 (8.3%)
- Aspirin + Clopidogrel	4 (3.0%)

*: Other indications include 3 bypass grafts, 1 mech valve replacement, 1 ventricular thrombus, and 1 venous graft after tumour resection.

†: Indications for anti-platelet prophylaxis might overlap, meaning one patient might have multiple of the listed comorbidities.

IQR indicates interquartile range; TIA, transient ischaemic attack; and VTE, venous thromboembolism.

Supplementary Table 4: Therapeutic management and outcomes of VTE under immune checkpoint inhibitor therapy

Agent Group	Agent	n (%)	Bleeding events	Recurrent VTE
DOAC	Apixaban	1		
	Edoxaban*	7	1 CRNMB	
	Rivaroxaban	5		1
LMWH	Dalteparin	1	1 MB	
	Enoxaparin	21	1 MB, 2 CRNMB	3
LMWH+DOAC†		8	1 CRNMB	
UFH‡		1		
None§		3		
Total		**47**	**4 CRNMB (8.5%)** **2 MB (4.3%) ‖**	**4 (8.5%) ¶**

*: with LMWH lead-in

†: Therapy changes include Enoxaparin to Apixaban (n=1, switch after 11 months), Enoxparin to Edoxaban (n=4, switch after 3, 3, 4, and 7 months), Enoxaparin to Rivaroxaban (n=2, switch after 1 month in both), Enoxaparin (3 months) to Rivaroxaban (1 dose), Dabigatran (1 dose) and Apixaban (n=1, CRNMB episode after Rivaroxaban and Dabigatran, respectively).

‡: UFH was used in patient who subsequently died due to suspected pulmonary embolism

§: No anticoagulation was applied due to fatal pulmonary embolism (n=1), bleeding risk (n=1) or death unrelated to VTE shortly after the index event (n=1).

‖: MB: 1 patient with gastrointestinal haemorrhage from colonic metastasis and 1 patient with an episode of epistaxis, each resulting in the transfusion of two units of red blood cells. CRNMB: 2 patients with large hematomas leading to repeated clinical evaluation, 1 patient with multiple episodes of macrohematuria, and 1 patient with epistaxis leading to otorhinolaryngologic consultation and gingival bleeding leading to switch in anticoagulation.

¶: VTE recurrence occurred at 1.5, 4.2, 9.4 and 9.7 months after the index event, respectively.

CRNMB indicates clinically relevant non-major bleeding; DOAC, direct oral anticoagulants; LMWH, low molecular weight heparin; MB, major bleeding; UFH, unfractionated heparin; and VTE, venous thromboembolism.

References

1. Seymour L, Bogaerts J, Perrone A, et al. iRECIST: guidelines for response criteria for use in trials testing immunotherapeutics. *The Lancet Oncology.* 2017;18(3):e143-e152.
2. Schulman S, Kearon C. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. *Journal of thrombosis and haemostasis : JTH.* 2005;3(4):692-694.
3. Kaatz S, Ahmad D, Spyropoulos AC, Schulman S, Anticoagulation tSoCo. Definition of clinically relevant non-major bleeding in studies of anticoagulants in atrial fibrillation and venous thromboembolic disease in non-surgical patients: communication from the SSC of the ISTH. *Journal of Thrombosis and Haemostasis.* 2015;13(11):2119-2126.